What is claimed is:

1. A method for producing a mixed acid anhydride of formula (1):

$$R^1C(O)OY(O)_n(R^2)_p \quad (1)$$

wherein R^1, R^2, Y, n and p denote the same as defined below, which comprises adding

a carboxylic acid of formula (2);

$$R^1COOH \quad (2)$$

wherein R^1 denotes

a hydrogen atom,

an optionally substituted saturated or unsaturated hydrocarbyl group, or

an optionally substituted hetero ring, and

an organic base to a solution of a carboxylic acid activating agent of formula (3);

$$(R^2)_p\ Y(O)_nX \quad (3)$$

wherein R^2 denotes

an optionally substituted alkyl group,

an optionally substituted aryl group,

an optionally substituted chain or cyclic alkoxy group, or

an optionally substituted aryloxy group,

Y denotes

a carbon atom, a phosphorus atom, or a sulfur atom,

X denotes

a fluorine atom, a chlorine atom, a bromine atom, an iodine atom, a cyano group or a group of formula:

$$(R^2)_p\ Y(O)_nO\cdot,$$

wherein R^2 is the same as defined above,

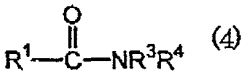
n and p are an integer of 1 or 2; and

when Y is a carbon atom, n=1 and p=1,

when Y is a phosphorous atom, n=1 and p=2, and

when Y is sulfur atom, n=2 and p=1 and R^2 denotes an optionally substituted alkyl or aryl group.

2. A method for producing an amide compound of formula (4);



(4)

wherein R^1 denotes

a hydrogen atom,

an optionally substituted saturated or unsaturated hydrocarbyl group, or

an optionally substituted hetero ring,

R^3 and R^4 independently denote

a hydrogen atom,

an optionally substituted saturated or unsaturated hydrocarbyl group,

an optionally substituted hetero ring,

a protective group for an amino group, or

R^3 represents a group of formula: $-OR^{30}$, or $-NR^{30}R^{31}$, wherein R^{30} represents an optionally substituted alkyl group, or an optionally substituted aryl group and R^{31} represents a hydrogen atom or an optionally substituted aryl group, and

R^3 and R^4 may be bonded to form a ring,

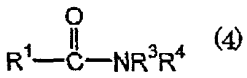
which comprises

reacting the mixed acid anhydride of formula (1) obtained as claimed in claim 1; with an amine of formula (5);

$$NHR^3R^4 \quad (5)$$

wherein R^3 and R^4 independently denote the same as described above.

3. A method for producing an amide compound of formula (4);



(4)

wherein R^1 denotes the same group as described below,

R^3 and R^4 independently denote

a hydrogen atom,

an optionally substituted saturated or unsaturated hydrocarbyl group,

an optionally substituted hetero ring,

a protective group for an amino group, or

R^3 represents a group of formula: $-OR^{30}$, or $-NR^{30}R^{31}$, wherein R^{30} represents an optionally substituted alkyl group, or an optionally substituted aryl group and R^{31} represents a hydrogen atom or an optionally substituted aryl group, and

R^3 and R^4 may be bonded to form a ring,

which comprises reacting a mixed acid anhydride obtained by adding a carboxylic acid of formula (2);

$$R^1COOH \quad (2)$$

wherein R^1 denotes

a hydrogen atom,

an optionally substituted saturated or unsaturated hydrocarbyl group, or

an optionally substituted hetero ring, and

an organic base to a solution of a carboxylic acid activating agent, and reacting the resulting mixed acid anhydride with an amine of formula

(5);

$$NHR^3R^4 \quad (5)$$

wherein R^3 and R^4 independently denote the same as described above, optionally in the presence of a base.

4. A method according to 3, wherein the carboxylic acid anhydride is a phosphonic acid trimer.

5. A method according to claim 1, 2 or 3, wherein

R^1 denotes

a hydrogen atom,

a straight, branched or cyclic (C1-C18)alkyl group,

a (C2-C5)alkenyl or (C5-C6)cycloalkenyl group,

a (C3-C4) alkynyl group,

a phenyl, tolyl, biphenyl and naphthyl group,

an aralkyl, arylalkenyl or arylalkynyl group,

a pyridyl group, a 1,3-oxazole group, a 1,3-thiazole group, a furyl group, a tetrahydrofuryl group, a thienyl group, an imidazole or (C2-C11)alkyleneimine group of which nitrogen atoms are protected by a protecting group,

wherein said groups other than hydrogen atom may be substituted with

(a) a hydroxy group or a halogen atom, or

(b) an amino group of formula: $R^{11}R^{12}N$- and optionally further with

at least one group selected from

a carbamoyl group, a methylmercapto group,

a 4-pyrimidinone-3-yl group,

an alkyl(C1-C3)dithio group, of which alkyl is substituted with an amino and carboxyl groups,

a mercapto, guanidyl, carboxyl, hydroxy or imidazolyl group,

wherein R^{11} represents a hydrogen atom or an amino–protecting group, R^{12} represents an amino-protecting group, or a group of formula: R^{13}-CO,

wherein R^{13} represents a saturated or unsaturated hydrocarbyl group or a hetero ring, which may be substituted with

(c) a hydroxy group, or a halogen atom, or

(d) a group of formula: $R^{14}R^{15}N$- and optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group,

an alkyl(C1-C3)dithio group, of which alkyl is substituted with an amino and carboxyl groups,

an amino, mercapto, guanidyl, carboxyl, hydroxy, imidazolyl group,

wherein R^{14} is an amino–protecting group, and R^{15} represents a hydrogen atom, a saturated or unsaturated hydrocarbyl group, a hetero ring or an amino-protecting group,

R^3 and R^4 independently denote

a chain, branched or cyclic (C1-C18)alkyl group,

a (C2-C5)alkenyl or (C5-C6)cycloalkenyl group,

a (C3-C4)alkynyl group,

a phenyl, tolyl, biphenyl and naphthyl group,

an aralkyl, arylalkenyl or arylalkynyl group,

a hetero ring selected from a pyridyl group, a 1,3-oxazole group, a 1,3-thiazole group, a furyl group, a tetrahydrofuryl group, a thienyl group, an imidazole or a (C2-C11)alkyleneimine group of which nitrogen atoms are protected by a protecting group,

all of which may be substituted with at least one group selected from

a halogen, nitro, (C1-C3)alkoxy, (C1-C3)alkyl, hydroxy, cyano

group, or (2-alkoxyiminoacetate)-2-yl group,

a carbamoyl group, a methylmercapto group,

an alkyl(C1-C3)dithio group, of which alkyl is substituted with a protected amino and carboxyl groups,

an amino, mercapto, guanidyl, carboxyl, hydroxy, imidazolyl group,

a group of formula: $C(O)-R^8$,

wherein R^8 is an alkoxy group or a group of formula: NHR^{80} wherein R^8 and R^{80} represents a saturated or unsaturated hydrocarbyl group or the hetero ring, both of which may be substituted with

a group of formula: $C(O)R^{81}$ or a hydroxy group and optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group,

alkyl(C1-C3)dithio group, of which alkyl is substituted with an amino and carboxyl groups,

an amino, mercapto, guanidyl, carboxyl, hydroxy, or imidazolyl group,

wherein R^{81} is an alkoxy group or a group of formula: NHR^{82} wherein R^{81} and R^{82} represent a saturated or unsaturated hydrocarbyl group or a hetero ring,

R^3 may represent a group of formula: $-OR^{30}$, or $-NR^{30}R^{31}$, wherein R^{30} represents an optionally substituted alkyl group, or an optionally substituted aryl group and R^{31} represents a hydrogen atom or an optionally substituted aryl group, and

R^3 and R^{40} may represent a hydrogen atom, or a protective group for an amino group,

provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may present in R^1, R^2, R^3 and substituent groups contained therein are in a protected form.

R^3 and R^4 may be bonded to form a ring,

R^2 denotes

a chain, branched or cyclic (C1-C6)alkyl group, which may be substituted with a halogen atom,

a phenyl which may be substituted with a halogen or (C1-C3)alkyl group,

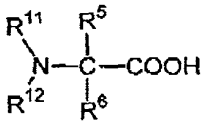
a chain or cyclic (C1-C6)alkoxy group, or

a phenoxy group which may be substituted with a halogen or C1-C3 alkyl group.

6. A method according to claim 5, wherein R^1 represents a group of formula (6): $R^{11}R^{12}N\text{-}A\text{-}$ (6)

wherein R^{11} and R^{12} are the same as defined in claim 5, and "A" represents an alkylene group, an alkenylene group, an alkynylene group, an arylene group, an aralkylene group, arylalkenylene group, arylalkynylene group, an oxazole ring, a thiazole ring, or an imidazole ring

7. A method according to claim 2 or 3, wherein said carboxylic acid defined by said general formula (1) is an α-amino acid derivative of formula (7):



(7)

wherein R^5 and R^6 represent a hydrogen atom or a saturated or unsaturated hydrocarbyl group or a hetero ring, both of which may be each substituted with

(a) a hydroxy group or a halogen atom, or

(b) at least one group selected from

a carbamoyl group, a methylmercapto group,

an alkyl(C1-C3)dithio group, of which alkyl is substituted with a

protected amino and carboxyl groups, and

an amino, mercapto, guanidyl, carboxyl, hydroxy or imidazolyl group,

R^{11} is a hydrogen atom or an amino–protecting group,

R^{12} represents an amino-protecting group or a group of formula: $R^{13}CO$-, wherein R^{13} represents a saturated or unsaturated hydrocarbyl group or the hetero ring, which may be substituted with

(c) a hydroxy or a halogen atom, or

(e) a group of formula: $R^{14}R^{15}N$- and optionally further with at least one group selected from

a carbamoyl group, a methylmercapto group,

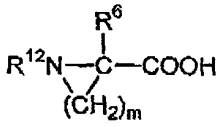
alkyl(C1-C3)dithio group, of which alkyl is substituted with a protected amino and carboxyl groups,

an amino, mercapto, guanidyl, carboxyl, hydroxy, or imidazolyl group, wherein R^{14} is an amino–protecting group, R^{15} represents a hydrogen atom or an amino-protecting group, and

R^{11} and R^{12}, and R^{14} and R^{15} may independently form an alkyleneimie group, a 4-pyrimidinone-3-yl group or the like,

provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R^{11}, R^{12}, R^5 and R^6 or substituent groups contained therein are in a protected form.

8. A method according to claim 5, wherein said carboxylic acid defined by the formula (7) is a cyclic α-amino acid derivative of formula (8);



(8)

wherein R^{12} and R^6 independently denote the same as defined in claim 5, and m denotes an integer from 1 to 10.

9. The method according to any one of claims 1 to 3, wherein said carboxylic acid activating agent defined by said formula (2) is an acid chloride (X = Cl).

10. The method according to any one of claims 1 to 3, wherein the amount of the organic base is 0.9 to 2 moles per mol of said carboxylic acid in the production of the mixed acid anhydride defined by said general formula (3).

11. The method according to claims 1 or 2, wherein the amount of the carboxylic acid activating agent is 0.95 to 1.05 moles per mol of the carboxylic acid.

12. The method according to claim 1 or 2, wherein the amount of the amine is 0.95 to 1.05 mol per mol of the carboxylic acid of formula (2).

13. The method according to claim 1, wherein the amount of the base per mol of the carboxylic acid of formula (2) is substantially equimolar.

14. The method according to claim 1 or 2, wherein the base is N-methylmorpholine.

15. The method according to claim 1, wherein the base and the carboxylic acid are simultaneously added.

16. The method according to claim 2, wherein the mixed acid anhydride formed after completion of the addition of the base and carboxylic acid is maintained for 30 minutes, and then reacted with the base to form the amide.